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10/070,568	03/08/2002	You-Min Feng	GJE-88	7193

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EXAMINER	
GUPTA, ANISH	
ART UNIT	**PAPER NUMBER**
1654	

DATE MAILED: 11/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/070,568	FENG ET AL.
	Examiner	Art Unit

-- Th MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) 1-17 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1,2,4,6,8,10,12,14 and 16 is/are rejected.

7)☒ Claim(s) 3,5,7,9,11,13,15 and 17 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 0502 .
4) ☒ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The Amendment filed 3-8-02 is acknowledged. Claims 1-5 were amended and claims 6-17 were added. Claims 1-17 are pending in this Application. Note, that the issue of pending claims was resolved as per the interview summary attached.

Claim Objections

2. Claims 1-17 objected to because of the following informalities:

Claim 1 says B1 and B30. Although it is recognized that B1 and B30 refer to the first and 30th position of the B chain, Applicants are requested to specifically state that B1 and B30 refer to the said positions in the B-chain, especially in all independent claims.

In claim 1, instead of stating " and which optionally also comprises deletion of B1 (phe) and/or B30 (thr)," Applicants are requested to state "which optionally also comprises deletion of either one or both of Phe at position 1, B1, or Thr at position 30, B30, of the B-chain of human insulin. This would also be applicable to claim 7 and 13.

In the claims, Applicants are requested to recite Tyr instead of (Tyr) to make the reference to amino acids more uniform.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Slieker et al.

The claims are drawn to a insulin analog wherein there are modifications at position 16 and 26 of the B-chain, with the replacement of tyrosine with alanine, and optionally deleting the amino acid in the B1 or B30 position in the B-chain of insulin.

The reference teaches an insulin analog wherein the tyrosine residue in position 26 of the B chain is replaced with Alanine (see page S56, Table 1). The reference states that the insulin analog modified is a human insulin analog (see abstract). The reference teaches all of the limitations of the claims 1 and 2 and therefore anticipated the claims. Note that the claims state that B1 and B30 are optionally deleted. Thus, the claims are still anticipated even with the presence of B1 and B30 amino acids since the deletion limitation is an option and not a requirement.

2. Claims 1-2, 6, 8, 12, 14 rejected under 35 U.S.C. 102(b) as being anticipated by Chance et al. (WO9414461).

The claims are drawn to a insulin analog wherein there are modifications at position 16 and 26 of the B-chain, with the replacement of tyrosine with alanine, and optionally deleting the amino acid in the B1 or B30 position in the B-chain of insulin, pharmaceutical formulations thereof, and method of treatment of insulin deficiency by administering the analogs.

The reference teaches modified insulin analogs that have modification at various positions including position 26 in the B-chain. The reference specifically teaches Ala (B26) human insulin wherein the tyrosine residue has been replaced by alanine (see page 5, lines 32-33). Further, the reference teaches the analogs are generally monomeric in solution and have rapid onset of activity one administered (see page 6, lines 5-8). There are disclosed pharmaceutical formulations, meeting

the limitations of claims 12 and 14, such as zinc, sodium, potassium or calcium salts (see page 6, lines 10-12). Finally, the reference teaches that the analog is useful in the treatment of hyperglycemia and diabetes, where deficiency of insulin is the most important factor in the disease state (see page abstract and page 1, lines 1-15). This meets the limitation of claims 6 and 8. Therefore, the reference anticipates the claimed invention. Note that the claims state that B1 and B30 are optionally deleted. Thus, the claims are still anticipated even with the presence of B1 and B30 amino acids since the deletion limitation is an option and not a requirement.

3. Claims 1-2 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Kristensen et al.

The claims are drawn to a insulin analog wherein there are modifications at position 16 and 26 of the B-chain, with the replacement of tyrosine with alanine, and optionally deleting the amino acid in the B1 or B30 position in the B-chain of insulin.

The reference teaches 21 different insulin analogs wherein an alanine residue was replaced in different positions of the Insulin A or B chain (see abstract and page 12979). Two of the analogs disclosed are Ala-B16 Insulin and Ala-B26 Insulin (see page 12979 and 12982 second column). The sequence disclosed in the reference corresponds to the human insulin analog (see page 12981). The reference teaches all of the limitations of the claims 1-2 and 4 and therefore anticipated the claims. Note that the claims state that B1 and B30 are optionally deleted. Thus, the claims are still anticipated even with the presence of B1 and B30 amino acids since the deletion limitation is an option and not a requirement.

Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 6, 8, 10, 12, 14, 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kristensen et al. as applied to claims 1-2 and 4 above, and further in view of Chance et al.

The claims are drawn to a insulin analog wherein there are modifications at position 16 and 26 of the B-chain, with the replacement of tyrosine with alanine, and optionally deleting the amino acid in the B1 or B30 position in the B-chain of insulin.

The reference of Kristensen et al. has been discussed supra. The reference also teaches that the B16 and B26 modified analogs altered affinity for the insulin receptor moderately (see page 12982). The difference between the prior art and the instant application is that Kristensen et al. does not teach the method of treating an individual having insulin deficiency and pharmaceutical composition.

However, Chance et al. teach pharmaceutical formulations of insulin analogs for the treatment of individuals with insulin deficiency. Since the reference of Kristensen et al. teach that modified analogs altered affinity for the insulin receptor moderately it would have been obvious to one of ordinary skill in the art to make pharmaceutical formulations to either treat insulin deficiency in a subject or to use the formulation in a study to see the effects of the B16 analog in insulin deficiency study. One would be motivated since Chance discloses the effectiveness of B26 alanine modified analog in the treatment of insulin deficiency which was also noted to have altered affinity for the insulin receptor.

5. Claims 3, 5, 7, 9, 11, 13, 15 and 17 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The claims are objected to because the prior art does not teach nor suggest the combination of modification of the in position B16 or B26 AND the deletion of B30 or B1 in the b-chain of the insulin. The prior art only teaches either modification or deletion but not both.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (703) 308-4001. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback , can normally be reached on (703)306-3220. The fax phone number of this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

10/17/05

Anish Gupta
Patent Examiner